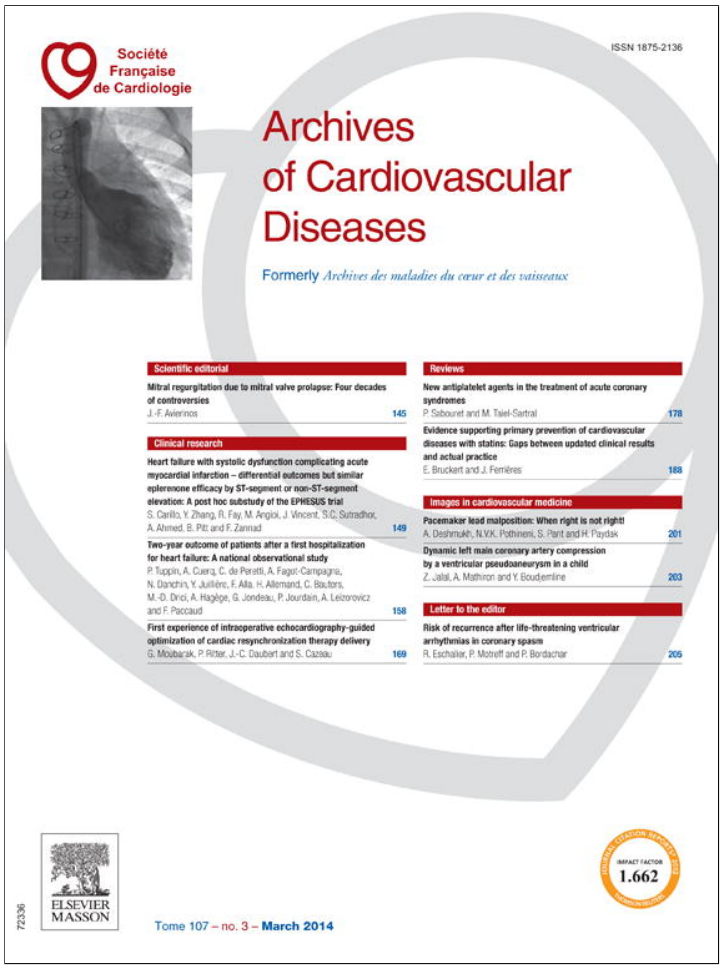

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CLINICAL RESEARCH

Two-year outcome of patients after a first hospitalization for heart failure: A national observational study

Devenir à deux ans après une première hospitalisation pour insuffisance cardiaque : une étude observationnelle nationale

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KEYWORDS
Heart failure;
Incidence;

Summary
Background. — National population-based management and outcome data for patients of all ages hospitalized for heart failure have rarely been reported.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AD, associated diagnosis; ALD, *affections de longue durée* (chronic diseases); ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; CI, confidence interval; ICD-10, tenth International Classification of Diseases; PD, principal diagnosis; RR, relative risk; SNIIRAM, *Système national d'information inter-régimes de l'assurance maladie* (French national interscheme health insurance information system).

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Hospitalization;
France;
SNIIRAM

Aim. — National population-based management and outcome of patients of all ages hospitalized for heart failure have rarely been reported. The present study reports these results, based on 77% of the French population, for patients hospitalized for the first time for heart failure in 2009.
Methods. — The study population comprised French national health insurance general scheme beneficiaries hospitalized in 2009 with a principal diagnosis of heart failure, after exclusion of those hospitalized for heart failure between 2006 and 2008 or with a chronic disease status for heart failure. Data were collected from the national health insurance information system (SNIIRAM).
Results. — A total of 69,958 patients (mean age, 78 years; 48% men) were studied. The hospital mortality rate was 6.4%, with 1-month, 1-year and 2-year survival rates of 89%, 71% and 60%, respectively. Heart failure and all-cause readmission-free rates were 55% and 43% at 1 year and 27% and 17% at 2 years, respectively. Compared with a reference sample of 600,000 subjects, the age- and sex-standardized relative risk of death was 29 (95% confidence interval [CI] 28—29) at 2 years, 82 (95% CI 72—94) in subjects aged < 50 years and 3 (95% CI 3—3) in subjects aged ≥ 90 years. For subjects aged < 70 years who survived 1 month after discharge, factors associated with a reduction in the 2-year mortality rate were: female sex; age < 55 years; absence of co-morbidities; and use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, beta-blockers, lipid-lowering agents or oral anticoagulants during the month following discharge. Poor prognostic factors were treatment with a loop diuretic before or after hospitalization and readmission for heart failure within 1 month after discharge.
Conclusions. — This large population-based study confirms the severe prognosis of heart failure and the need to promote the use of effective medications and management designed to improve survival.

MOTS CLÉS
Insuffisance cardiaque ;
Incidence ;
Hospitalisation ;
France ;
SNIIRAM

Résumé
Contexte. — La prise en charge et le devenir de patients hospitalisés pour insuffisance cardiaque (IC) à un niveau national et tous âges confondus, est rarement rapporté.
Objectif. — C'est le cas de cette étude sur 77 % de la population française pour des patients avec une première hospitalisation pour IC en 2009.
Méthodes. — Parmi les bénéficiaires du régime général de l'Assurance maladie hospitalisés en 2009 avec un diagnostic principal d'IC ont été exclus ceux hospitalisés pour IC entre 2006 et 2008 ou avec une affection de longue durée pour IC. Les données utilisées étaient celles présentes dans le système d'information de l'Assurance maladie (SNIIRAM).
Résultats. — Au total, 69 958 patients ont été inclus (âge moyen 78 ans, 48 % d'hommes). Leur taux de décès hospitalier était de 6,4 %. Leurs taux de survie étaient de 89 % à un mois, 71 % à un an et de 60 % à deux ans. Ceux sans réhospitalisation pour IC étaient de 55 % à un an et de 43 % à deux ans et sans réhospitalisation toutes causes respectivement de 27 % et 17 %. Comparativement à un échantillon permanent par tirage au sort de 600 000 assurés, leur risque relatif de décès à 2 ans, standardisé sur l'âge et le sexe, était de 29 (95 % CI 28—29) et chez les moins de 50 ans de 82 (95 % CI 72—94) et de 3 (95 % CI 3—3) chez ceux de 90 ans et plus. Pour les moins de 70 ans ayant survécu un mois après leur sortie, les facteurs positifs associés au décès à deux ans étaient le sexe féminin, l'âge inférieur à 55 ans, l'absence de comorbidités, une consommation le mois de sortie d'IEC-sartan, de bêtabloquant, d'hypolipémiant, d'anticoagulant oral. Parmi les facteurs péjoratifs, il était retrouvé un traitement par diurétique de l'anse avant ou après hospitalisation et une réhospitalisation pour IC le mois de sortie.
Conclusion. — Cette étude sur une large population confirme la sévérité du pronostic de l'IC, la nécessité de favoriser l'utilisation de médicaments bénéfiques et de prises en charge limitant les réhospitalisations.

Background

Heart failure is a disabling and complex syndrome, with a high prevalence (2% of the Western population, 10% after the age of 75 years) that is still increasing, together with the associated healthcare consumption [1—4]. Nevertheless, standardized hospitalization rates for heart failure are globally tending to decline in several countries, such as France, but the readmission rate remains high [2,5—8]. In the USA, the proportion of Veterans readmitted to hospital within 30 days following discharge was 5.6% for heart failure and 22% for all causes (2002—2006) — similar to the 23%

readmission rate for Medicare beneficiaries (2004—2006) [9,10]. In France, 21% of all patients hospitalized for heart failure in 2008 were readmitted to hospital at least once for heart failure during the same calendar year. Early readmissions for heart failure have multiple causes, and therapeutic patient education and management programmes are recommended at the time of discharge from hospital [11,12]. An improvement in survival has been reported, particularly after a first hospitalization, but the prognosis nevertheless remains poor [7,13,14]. Reported survival rates vary according to the period and the mode of patient selection, but also to sociodemographic and clinical case mixes [1,3,4]. Patients with heart failure have a high mortality rate compared with the general population, but this has rarely been compared by sex and age group in large populations [15]. Clinical trials have demonstrated in specific age groups the benefit of a number of drugs in terms of survival, such as angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and beta-blockers, even if their use is suboptimal [12,16,17].

This observational study in patients of all ages derived from a large comprehensive population (77% of the French population) hospitalized for the first time for heart failure in 2009 and followed for 2 years, aimed to determine the readmission and mortality rates compared with a reference population and to assess factors associated with mortality among survivors after hospital discharge.

Methods

Information system and population

In France, the *Système national d'information inter-régimes de l'assurance maladie* (SNIIRAM; French national inter-scheme health insurance information system) comprises an individual and anonymous database concerning the beneficiaries of the various schemes [18]. The database comprehensively records all outpatient prescriptions, services and procedures performed and reimbursed, together with their dates. Historical data are limited to a period of 3 years plus the current year. Medications are identified according to Anatomical Therapeutic Classification (ATC) code and laboratory tests are identified from the French national laboratory test coding table. Although the database does not contain any clinical information concerning the results related to prescriptions or examinations, it nevertheless indicates the presence of any ''*affections de longue durée*'' (ALD; chronic diseases), eligible for 100% reimbursement of healthcare expenditure, such as cardiovascular diseases, after application by the attending physician and approval by the national health insurance consultant physician. An anonymous unique identification number for each subject links this information to data collected by the national hospital discharge database (PMSI: *Programme de médicalisation des systèmes d'information*) in public and private healthcare institutions. During the patient's stay, principal diagnoses (PDs), associated diagnoses (ADs) and any ALD chronic diseases are coded according to the tenth International Classification of Diseases (ICD-10). In parallel, this database also provides a permanent open randomized sample (*Échantillon Permanent des Bénéficiaires*) representing 1/97th of all national health insurance schemes beneficiaries (600,000 subjects) and one of the main advantages of this sample is the exhaustiveness of survival data.

The study population was limited to beneficiaries of the national health insurance general scheme (77% of the 64 million inhabitants in France in 2009), excluding those covered by local mutualist sections (students, civil servants, etc.), the *Mutualité Sociale Agricole*, the *Régime Social des Indépendants* and other specific health insurance. The reasons for limiting the study to this population were the availability of vital status and date of death from the National Institute for Statistics and Economic Studies (INSEE) for the general scheme in the SNIIRAM and the lack of completeness for some SNIIRAM characteristics in some other schemes. To optimally target first hospitalizations for heart failure, patients hospitalized with a PD of heart failure (ICD-10 code I50) in 2009, but not between 2006 and 2008, and also not presenting an ALD status for heart failure were selected for this study. Patients hospitalized in 2008 with an AD of heart failure were also excluded. Hospitalizations with the following PDs were not included: I11.0 hypertensive heart disease; I13.0 hypertensive heart and renal disease with (congestive) heart failure; I13.2 hypertensive heart and renal disease with (congestive) heart failure and renal failure; I13.9 hypertensive heart and renal disease, unspecified; K76.1 chronic passive congestion of liver; and J81 pulmonary oedema.

Definitions and statistical analysis

Patient characteristics and management

The search for co-morbidities before the first hospitalization for heart failure took into account the presence of specific chronic diseases identified by ICD-10 codes. Drug treatments were identified by the presence of at least three reimbursements during the 6 months preceding the index hospitalization and by a single reimbursement during the 30 days following discharge among patients still alive. The absence of all-class medications reimbursements during these two periods was also studied in order to identify, especially among the oldest patients, those living in an institution that manages medicinal products directly and for whom no information on drug consumption is therefore recorded in the SNIIRAM database. Reimbursements for hospital outpatient clinic and office visits were used to identify cardiology consultations. As echocardiography is not systematically coded during a cardiology visit, because the levels of reimbursement may be similar for a visit with or without echocardiography, a variable was constructed by combining the existence of at least one visit to the cardiologist or echocardiography.

Readmission, survival and risk factors associated with mortality

Survival rates were calculated for the overall patient population (including hospital deaths). The 2-year mortality was compared with that of the Échantillon Permanent des Bénéficiaires sample, with standardization according to sex and age, and calculation of relative risk (RR) and 95% confidence intervals (CIs). Readmissions were taken into account only when they occurred at least 7 days after discharge,

in order to avoid considering early transfers. Readmissions were studied according to the presence of a PD or AD of heart failure or an all-cause PD. Readmission-free survival rates (all-cause or heart failure) were also calculated. Readmission rates for heart failure were also calculated with censoring of deaths, i.e. based on all patients still alive at the end of the period considered. The presence of at least one readmission — or the first readmission — was reported according to the principal diagnoses coded and was grouped according to the main chapters of ICD-10 for patients still alive at 2 years.

To evaluate the available factors possibly associated with survival, the first step in the study consisted of descriptive analysis of the patients surviving 30 days after discharge and presenting at least one all-class medicinal product reimbursement 6 months before and 1 month after hospitalization. Univariate and then multivariable Cox models were used to identify factors independently associated with mortality between 1 month and 24 months after discharge, with calculation of the hazard ratio (HR). Two groups were considered (patients aged < 70 years and patients aged ≥ 70 years) in view of the age-related differences in patient characteristics, especially the proportions of the two types of heart failure. The standardized survival of these patients was also compared with that of patients excluded because of the absence of medicinal product reimbursement, who were likely to be institutionalized. SAS version 4.3 software was used (SAS Institute Inc, Cary, NC, USA).

Results

For the overall population of general scheme beneficiaries, 152,601 hospitalizations for heart failure were identified in 2009, corresponding to 130,333 patients; 69,958 (53%) of these patients were hospitalized for heart failure for the first time (48% men; mean age, 78 ± 3 years).

Survival

One and 2-year survival rates were 71% and 60%, respectively. One and 2-year survival rates without readmission for heart failure after hospital discharge were 55% and 43%, respectively, and without all-cause readmission were lower, at 27% and 17%, respectively (Table 1). First readmission rates for heart failure among those patients still alive at the end of the period considered were 5% at 1 month and 14% at 6 months and then stabilized to reach 16% at 2 years. Readmission rates for heart failure were higher in youngest patients, who also had the highest survival rates.

Mortality

The 2-year mortality rate was higher than that in a random sample of about 600,000 beneficiaries: 40% for all ages combined and 45.5% for patients aged ≥ 75 years (Fig. 1). The age- and sex-standardized RR of death was 29 (95% CI 28—29) for all patients hospitalized for heart failure, 31 (95% CI 30—32) for women and 27 (95% CI 26—28) for men. The RR was higher among the youngest patients and decreased with age: < 50 years, RR 82 (95% CI 72—94); 50—59 years, RR 17 (95% CI 15—19), 60—69 years, RR 12 (95% CI 11—13); 70—79

Table 1 Outcome of patients after a first hospitalization for heart failure in 2009, according to age.

	Time since discharge (months)			
	1	6	12	24
Survival[a] (%)				
All ages	89.2	78.3	70.8	59.7
< 55 years	96.3	91.9	88.8	84.6
55—69 years	94.7	88.6	84.0	77.1
70—79 years	92.6	83.7	77.4	68.0
80—89 years	87.2	74.6	65.7	52.3
≥ 90 years	78.5	60.6	49.7	34.3
Survival without readmission for heart failure (%)				
Total	84.6	64.7	54.8	42.6
< 55 years	91.5	77.5	70.0	64.5
55—69 years	89.4	73.9	64.9	56.4
70—79 years	87.8	68.9	59.5	48.5
80—89 years	82.8	61.6	51.0	36.9
≥ 90 years	75.0	49.6	38.8	24.4
Survival without readmission for all causes (%)				
Total	73.1	38.7	26.8	16.7
< 55 years	75.4	40.3	32.2	26.2
55—69 years	74.1	39.5	28.5	19.9
70—79 years	74.2	39.2	27.3	17.0
80—89 years	73.0	39.1	26.4	15.2
≥ 90 years	68.6	34.3	22.5	11.6
At least one readmission for heart failure without death (%)				
Total	4.6	13.6	15.8	16.5
< 55 years	4.8	14.4	16.4	18.5
55—69 years	5.3	14.7	17.5	19.4
70—79 years	4.9	14.8	17.5	19.5
80—89 years	4.4	13.0	15.2	15.2
≥ 90 years	3.5	11.1	12.0	12.4

[a] Including hospital deaths.

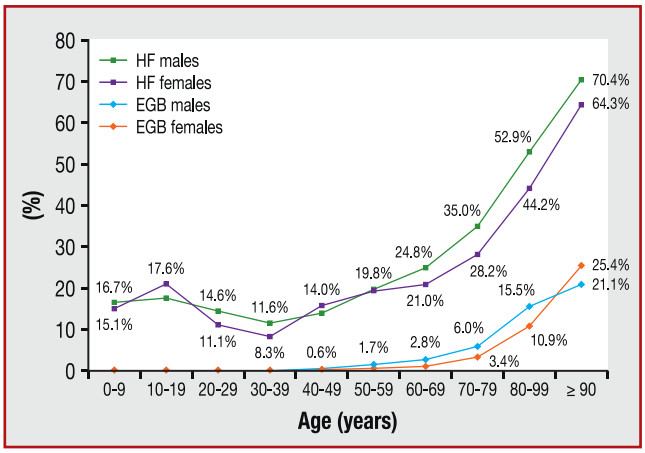

Figure 1. Age- and gender-adjusted 2-year mortality rates of patients with a first hospitalization for heart failure in 2009, compared with those of a random sample of national health insurance beneficiaries (EGB). HF: heart failure; EGB, *Échantillon Permanent des Bénéficiaires*.

years, RR 7 (95% CI 7—7); 80—89 years, RR 4 (95% CI 4—4); ≥ 90 years, RR 3 (95% CI 3—3).

Readmissions

The rate of at least one all-cause readmission among survivors was 69% and remained relatively stable according to age (Table 2). A diagnosis of heart failure was reported for 24% of first readmissions and another cardiovascular disease was reported for 22%, i.e. 46% overall for all cardiovascular diseases. The proportion of first readmissions for heart failure increased with age, whereas it decreased for other cardiovascular diseases. The proportion of readmissions for diseases of the respiratory system, symptoms and injury also increased according to age.

Patient characteristics and treatments

No medicinal products were reimbursed 6 months before hospitalization for 4.9% of all patients included, while no medicinal products were reimbursed for 12.7% of 30-day survivors after the first hospitalization and for 20% of patients aged ≥ 90 years (Table 3). A total of 53,168 patients were still alive at 1 month and had at least one all-class medicinal product reimbursed within 6 months before hospitalization and the month following hospitalization. These patients had a mean age of 77 ± 3 years, 51% were women and 74% presented at least one co-morbidity. During the year preceding hospitalization, 42% had had at least one brain natriuretic peptide (BNP) assay and 48% had been examined by echocardiography or had consulted a cardiologist. During the first month after discharge, 30% of patients had consulted a cardiologist, 79% had consulted their general practitioner and 17% had had at least one BNP assay.

Reimbursement rates for standard heart failure cardiovascular treatments within 6 months prior to before hospitalization were 40% for beta-blockers, 56% for ACEIs/ARBs, 60% for diuretics and 19% for aldosterone antagonists. Treatment frequencies 30 days after discharge were 54% for beta-blockers, 67% for ACEIs/ARBs, 85% for diuretics, 34% for aldosterone antagonists and 37% for the beta-blocker, diuretic and ACEI/ARB combination. Treatment with beta-blockers and ACEIs/ARBs was more frequent among

Table 2 Two-year outcome of survivors after a first hospitalization for heart failure in 2009 and principal diagnosis at the first readmission for 2-year survivors, according to age.

	Age (years)					All
	< 55	55—69	70—79	80—89	≥ 90	
Events						
Total number	4005	10 731	17 600	28 888	8734	69 958
Readmission[a] with or without death (%)	68.0	72.1	73.0	69.0	60.0	69.0
Death without readmission[a] (%)	5.8	8.0	10.0	15.8	28.4	14.3
Readmission[a] or death (%)	73.8	80.1	83.0	84.8	88.4	83.3
Principal diagnosis at the first readmission						
Total number	2721	7733	12 841	19 918	5237	48 306
Cardiovascular diseases (%)	55.2	52.8	46.9	43.4	42.9	46.3
Heart failure	20.9	20.5	22.6	26.2	30.2	24.5
Angina pectoris	1.5	2.4	2.2	1.4	1.1	1.7
Acute myocardial infarction	0.7	0.8	0.8	0.9	1.1	0.9
Chronic ischaemic heart disease	3.2	4.7	3.4	1.5	0.4	2.4
Cardiomyopathy	8.8	4.2	1.4	0.5	0.2	1.7
Atrial fibrillation and atrial flutter	6.0	7.3	4.6	2.7	1.4	4.0
Cerebral infarction	0.4	0.5	0.8	1.2	1.4	0.9
Other cardiovascular diseases	13.7	12.4	11.1	9.0	7.1	10.2
Tumours (%)	4.2	6.9	7.5	7.0	5.5	6.8
Endocrine diseases (%)	4.4	4.4	3.5	2.6	2.2	3.1
Diseases of the nervous system (%)	2.6	2.8	2.5	1.9	1.4	2.2
Diseases of the eye and adnexa (%)	0.4	2.3	3.7	3.4	1.5	2.9
Diseases of the respiratory system (%)	5.0	6.2	8.1	9.9	13.1	9.0
Diseases of the digestive system (%)	4.5	4.1	5.1	4.8	4.7	4.7
Diseases of the genitourinary system (%)	4.0	3.9	4.3	4.0	3.2	4.0
Symptoms, signs and abnormal clinical and laboratory findings (%)	5.7	5.4	6.6	8.0	9.2	7.3
Injury (%)	2.2	2.2	3.4	5.9	7.7	4.7
Factors influencing health status (%)	3.7	3.8	2.7	2.1	1.5	2.6
Other (%)	8.1	5.2	5.7	7.0	7.1	6.4
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0

[a] At least one all-cause readmission.

Table 3 Characteristics and management of 53,168 general scheme patients before and after a first hospitalization for heart failure in 2009[a], by age and sex.

	Age (years)					Women[b]	Men[b]	Total
	< 55	55–69	70–79	80–89	≥ 90			
Total number	4005	10 731	17 600	28 888	8734	33 408	36 550	69 958
No medicinal products reimbursed 6 months before (%)	12.3	7.4	3.7	3.7	5.4	4.7	5.2	4.9
Number surviving thirty days after discharge	3858	10 184	16 309	25 225	6841	32 365	30 052	62 417
No medicinal products reimbursed 30 days after discharge (%)	10.9	8.4	9.8	14.7	19.7	15.1	10.1	12.7
Number with ≥ one reimbursement 6 months before and 30 days after	3122	8810	14 444	21 317	5475	27 086	26 082	53 168
Mean age (years)						79.8	74.0	77.0
Women (%)	36.3	33.5	44.4	58.5	74.2			50.9
No ALD chronic disease (%)	46.8	27.7	21.7	24.2	31.4	28.0	24.2	26.1
ALD tumours (%)	5.3	10.1	13.5	13.1	10.0	10.4	13.5	11.9
Other ALD chronic disease (%)	20.2	18.6	17.2	16.2	15.9	18.4	15.7	17.1
12 months prehospitalization								
At least one cardiology consultation or echocardiography	48.5	53.3	54.5	46.4	31.1	43.6	53.2	48.3
At least one BNP assay	29.5	38.5	43.9	44.2	40.0	40.3	43.5	41.9
6 months prehospitalization								
ACEI/ARB	34.9	55.1	61.9	57.9	46.9	54.3	57.7	56.0
Beta-blocker	29.6	42.5	44.7	39.3	28.7	39.2	39.7	39.6
Diuretic (at least one)	31.8	50.8	61.9	65.5	62.6	60.6	59.4	59.8
Loop diuretic	25.2	37.2	45.8	50.6	51.6	44.3	47.7	45.7
Thiazide diuretic	6.3	15.6	19.2	17.6	12.9	18.9	14.0	16.5
Potassium-sparing diuretic	10.0	11.2	10.4	10.2	8.7	10.9	9.6	10.3
Potassium-sparing diuretic associated	8.3	9.8	9.2	8.9	7.5	9.5	8.3	8.9
During the first month posthospitalization								
At least one cardiology consultation or echocardiography	32.0	35.5	33.4	28.8	19.8	27.8	33.1	30.4
At least one GP consultation	68.7	73.9	80.2	82.0	82.8	81.3	77.5	79.5
At least one BNP assay	13.3	16.1	16.8	17.6	17.0	16.4	17.3	16.8
Beta-blockers	65.2	64.1	57.7	49.2	36.3	52.4	53.9	53.6
ARB	13.1	21.5	24.3	21.3	15.3	23.7	18.6	21.1
ACEI	61.6	55.4	48.9	42.9	36.3	43.0	50.5	47.0
ACEI or ARB	72.5	74.6	71.4	63.1	51.0	65.0	67.7	66.6
Diuretic (at least one)	75.5	82.8	86.4	86.8	85.1	85.0	85.6	85.2
Loop diuretic	70.4	77.4	81.5	83.0	82.9	80.2	81.8	80.9
Thiazide diuretic	5.4	9.2	9.3	7.3	4.6	8.8	6.9	7.8
Potassium-sparing diuretic	30.3	24.7	18.4	14.1	9.4	16.7	17.9	17.5
Potassium-sparing diuretic associated	27.7	23.1	17.3	13.3	9.0	15.8	16.7	16.4

Table 3 (*Continued*)

	Age (years)					Women[b]	Men[b]	Total
	< 55	55—69	70—79	80—89	≥ 90			
Potassium	25.6	29.5	31.7	34.2	33.6	32.9	31.3	32.2
Calcium channel blocker	13.4	22.1	25.5	23.9	22.4	24.4	22.0	23.3
Cardiotonic steroid	8.1	10.3	11.5	13.5	14.2	13.7	10.4	12.2
Class III antiarrhythmic	15.0	24.2	27.0	24.7	20.0	23.2	24.8	24.2
Oral anticoagulant	28.0	36.6	43.2	41.0	23.0	37.8	38.5	38.3
Platelet aggregation inhibitor	37.1	50.9	48.9	45.3	49.8	41.5	52.5	47.2
Lipid-lowering agent	33.1	54.2	52.9	37.8	16.3	37.1	47.0	42.1
Antidiabetics	16.8	34.9	33.2	20.8	10.2	25.5	25.2	25.2
Combinations								
ACEI/ARB only	2.9	2.9	2.5	2.6	3.0	2.7	2.7	2.7
Beta-blocker only	3.1	2.6	2.2	1.8	1.7	2.3	2.0	2.1
Diuretic only	8.7	8.6	11.0	16.3	25.6	14.7	13.8	14.1
ACEI/ARB + diuretic	13.4	18.8	23.8	25.7	26.6	23.6	23.7	23.4
ACEI/ARB + beta-blocker	8.8	6.1	3.9	2.6	1.6	3.5	3.9	3.8
Beta-blocker + diuretic	6.0	8.6	10.4	12.6	13.2	11.5	10.7	11.0
Beta-blocker + ACEI/ARB	47.3	46.9	41.2	32.2	19.8	35.1	37.4	36.7

ACEI: angiotensin-converting enzyme inhibitor; ALD: *affections de longue durée* (chronic diseases); ARB; angiotensin receptor blocker; BNP: brain natriuretic peptide; GP: general practitioner.
[a] Among patients surviving at least 30 days after discharge with at least one all-class medicinal product reimbursement during these 30 days and during the 6 months preceding hospitalization.
[b] Adjustment for age.

the youngest patients (64% and 75% in the 55—69 years age group, respectively).

Factors associated with mortality between 1 and 24 months

This analysis concerned the 53,168 survivors at 1 month with at least one medicinal product reimbursement (Table 4). Favourable prognostic factors on multivariate analysis for patients aged < 70 years were: female sex; aged < 55 years; absence of ALD chronic disease; and, 1 month after discharge, treatment with ACEI/ARB, beta-blocker, lipid-lowering agent, oral anticoagulant or calcium channel blocker and at least one cardiology consultation or echocardiography. Poor prognostic factors included the presence of an ALD chronic disease status for tumour, treatment with a loop diuretic before and/or after hospitalization and, 1 month after discharge, readmission for heart failure and at least one BNP assay. These factors were similar for patients aged ≥ 70 years, but with lower hazard ratio values. Notable supplementary favourable prognostic factors in this older population were diabetes and at least one BNP assay during the year preceding hospitalization; poor prognostic factors were at least one cardiology consultation or echocardiography during the year preceding hospitalization.

Patients surviving at 1 month with no medicinal product reimbursement were more likely to be women (62% vs 50%) and older (mean age, 79 years vs 77 years). After adjustment, 6-month, 1-year and 2-year mortality rates were 21%, 30% and 43%, respectively. These rates were significantly higher than those in patients with at least one medicinal product reimbursement during the month after discharge (11%, 20% and 33%, respectively).

Discussion

This large-scale real-life study of 69,958 patients hospitalized for the first time for heart failure revealed a high mortality rates in this population: 6.4% in hospital, 11% at 1 month, 29% at 1 year and 40% at 2 years. The 2-year mortality rate was 29-fold higher than that in a large control sample.

Mortality

An improvement in the short-term hospital mortality of heart failure has been reported in the United States among Veterans (mean age, 70 years; 2002—2006) and Medicare patients (mean age, 80 years; 1993—2006), with mortality rates during the first hospitalization of about 2.8% among Veterans and 4.3% among Medicare patients [9,19]. These rates are lower than the 6.4% mortality rate observed in our study, which only considered the first hospitalizations of patients with a mean of age of 78 years, and the 10.4% mortality rate observed in Canada in 2004 among patients aged ≥ 20 years [20]. Although the mean length of hospital stay is decreasing in the USA, an increased rate of transfer to long-stay or rehabilitation units has also been observed. The mean length of stay was 6 days for Medicare beneficiaries hospitalized in 2008 versus 9 days for a first hospitalization, regardless of age, in our previous study conducted in the

Table 4 Factors associated with mortality between 1 and 24 months among general scheme patients with a first hospitalization for heart failure in 2009[a], according to age (Cox models).

	< 70 years (n = 11 932)				≥ 70 years (n = 41 236)			
	HR	CIL	CIU	P	HR	CIL	CIU	P
55—69 vs < 55 years	1.3	1.2	1.5	***	—	—	—	
80—89 vs 70—79 years					1.6	1.5	1.6	***
≥ 90 vs 70—79 years		—			2.4	2.3	2.6	***
Women	0.8	0.7	0.9	***	0.8	0.7	0.8	***
No ALD chronic disease	0.6	0.5	0.7	***	0.8	0.8	0.8	***
ALD tumours	2.0	1.8	2.3	***	1.2	1.2	1.3	***
Other ALD chronic disease	1.3	1.1	1.4	***	1.1	1.1	1.2	***
12 months prehospitalization								
At least one cardiology consultation or echocardiography					0.9	0.8	0.9	***
At least one BNP assay					1.1	1.0	1.1	***
6 months prehospitalization								
Beta-blocker					0.9	0.9	1.0	***
Loop diuretic	1.5	1.4	1.7	***	1.4	1.3	1.4	***
Thiazide diuretic					0.9	0.9	1.0	**
Potassium-sparing diuretic					1.1	1.0	1.2	***
First 30 days posthospitalization								
ACEI/ARB	0.7	0.6	0.7	***	0.8	0.8	0.8	***
Beta-blocker	0.7	0.7	0.8	***	0.9	0.9	1.0	***
Loop diuretic	1.3	1.2	1.5	***				
Thiazide diuretic					0.9	0.8	0.9	***
Calcium channel blocker	0.9	0.8	1.0	*	0.9	0.8	0.9	***
Oral anticoagulant	0.8	0.8	0.9	***	0.8	0.8	0.9	*
Platelet aggregation inhibitor					1.0	1.0	1.1	***
Lipid-lowering agent	0.9	0.8	0.9	**	0.8	0.8	0.8	***
At least one readmission for heart failure	1.8	1.6	2.0	***	1.7	1.6	1.8	*
At least one GP consultation					1.0	1.0	1.1	***
At least one cardiology consultation or echocardiography	0.9	0.8	1.0	**	0.8	0.8	0.9	*
BNP assay	1.2	1.1	1.4	**				

ACEI: angiotensin-converting enzyme inhibitor; ALD: affections de longue durée (chronic diseases); ARB; angiotensin receptor blocker; BNP: brain natriuretic peptide; CIL: confidence interval lower bound; CIU: confidence interval upper bound; GP: general practitioner; HR: hazard ratio.

[a] Among patients surviving at least 30 days after discharge with at least one all-class medicinal product reimbursement during these 30 days and during the 6 months preceding hospitalization.

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

same population [19,21]. This reduction in hospital mortality may therefore have an impact on the 30-day mortality rate regarding the reduction in mean length of stay. For example, the 30-day mortality rate in the USA was 8% among Veterans but 11% among Medicare beneficiaries in 2006, similar to the rate observed in the present study. In Scotland, the 30-day mortality rate after a first hospitalization for heart failure had decreased, but in 2003 it was still about 16% for patients with a similar mean age to those in the present study [7].

The 1-year mortality rate after a first hospitalization for heart failure was 29% in our study, higher than the 24% 1-year mortality rate reported in Scotland, where the early mortality rate was higher, and similar to the 30% 1-year mortality rate reported in the USA in 2008 for all hospitalizations for heart failure among Medicare beneficiaries [6,7]. In Worcester, USA, the 1-year and 2-year mortality rates after the first hospitalization for heart failure in 2000 for patients with a mean age of 76 years, close to that in our study, were 28% and 40%, respectively, similar to the rates observed in our study (29% and 40%) [22].

Few data are available concerning the highest 2-year mortality rate after a first hospitalization for heart failure. An Icelandic study conducted in a population of patients aged ≥ 57 years living in the community reported 1-year, 2-year, 5-year and 7-year mortality rates of 26%, 35%, 55%, 68%, respectively, versus 3%, 6%, 20% and 30%, respectively, for matched controls without heart failure, corresponding to an RR at 2 years of about 6, slightly less than the RR of 8 for this age group in our study [15]. Our study also reported a much higher mortality rate for the youngest

patients. Apart from the different pathophysiological settings of heart failure according to age, this phenomenon can also be attributed to differences in the frequency of co-morbidities between patients and controls. A previous study in this same population demonstrated high rates of coronary heart disease, cardiac arrhythmias and valvular heart disease, as well as other diseases, such as diabetes and malignant tumours (particularly breast and haematopoietic tissues), and higher rates of antipsychotic drug use among patients aged 55—69 years with heart failure [21]. In this study, readmissions for ischaemic heart disease, cardiomyopathy or arrhythmia, which can be responsible for systolic heart failure, were also more frequent among the youngest patients, and the highest HR was observed for at least one readmission for heart failure during the 30 days after discharge. In contrast, a poor survival rate was observed for institutionalized patients with no medicinal product reimbursements after standardization for sex and age. However, institutionalization of these patients could be justified by a higher rate of severe disability, co-morbidity and a poorer general state of health [23—25].

Readmissions

The national study on all hospitalizations for heart failure in France in 2008 reported a readmission rate for heart failure during the calendar year of 20%, and 75% of these readmissions occurred during the first 3 months after discharge. In the present study, 1-month and 1-year heart failure first readmission rates were 9% and 18%, and all-cause rates were 22% and 63%, respectively. The 1-month heart failure readmission rate among Veterans in the USA increased between 2002 and 2006, but was 6% in 2006 [9]. For Medicare patients, the 1-month all-cause readmission rate was similar to that in our study (22%) [19]. Compared with our study, the 1-year all-cause readmission rate was a little higher (63% vs 66%) for Medicare patients [23]. A study conducted in the USA in patients with a similar mean age to those in our study and with a mean follow-up of almost 5 years, reported that 40% of readmissions were due to cardiovascular disease versus 46% of first readmissions in our study [26]. Readmissions for other diagnoses, such as injury or diseases of the respiratory system, increased with age in our study and tended to worsen the prognosis of the heart failure and make management of heart failure, especially drug treatment, more difficult.

Treatments and management at 30 days

In this study based on a population with a mean age of 77 years, treatment frequencies 30 days after discharge were 54% for beta-blockers, 47% for ACEIs, 67% for ACEIs/ARBs, 85% for loop diuretics and 34% for aldosterone antagonists. The French FUTURE study conducted in 2008 did not observe any differences in treatment frequencies on discharge from hospital and at follow-up visits between patients with a left ventricular ejection fraction > 40% (44% of patients) or < 40% (56% of patients) [16]. Among these 1137 patients (mean age, 72 years) followed by an office cardiologist, 74% were treated with beta-blockers, 83% with an ACEI/ARB, 86% with a loop diuretic and 31% with an aldosterone antagonist. The French IMPACT RECO study in 2005, based on 2000 patients with New York Heart Association grade III and IV systolic heart failure (mean age, 70 years) followed by office cardiologists, revealed very similar treatment frequencies: 70% for beta-blockers, 68% for ACEIs and 30% for ARBs (i.e. 91% for ACEIs/ARBs), 85% for loop diuretics and 35% for aldosterone antagonists [17]. Treatment frequencies 30 days after discharge in the present study were therefore lower than those reported in the previous study. However, patients in our study were older (mean age, 77 years) and probably presented a higher rate of contraindications to the use of medicinal products, such as ACEIs or beta-blockers, or non-indication (co-morbidities, left ventricular ejection fraction, etc.). Treatment frequencies were also higher among the youngest patients.

Factors associated with mortality between 1 month and 24 months

The favourable effect on survival of follow-up by a cardiologist has already been reported and is now part of guidelines [27,28]. This effect can be explained by improved management, but also by a better state of health, allowing the patient to attend the visit with the cardiologist or, more rarely, a visit by the cardiologist to the patient's home or institution. This real-life study, like similar studies or clinical trials [12,22,24,25,29], demonstrated a beneficial effect of beta-blockers and ACEIs/ARBs on the survival of young subjects. Nevertheless, this effect was also observed in older patients, who are rarely recruited in clinical trials. However, older patients treated with these agents could be the subject of indication biases related to the pathophysiology of heart failure and their clinical state. Thiazide and potassium-sparing diuretics have a beneficial effect in these older patients, but the use of loop diuretics has a negative prognostic impact for the two age groups. These drugs may be prescribed for relief of symptoms, in accordance with guidelines, but they may also indicate a clinical stage associated with severe symptoms, reflecting more advanced disease [12].

Study limitations

Certain groups of the French population, such as civil servants, liberal professionals and farmers, were not included in this study due to their occupation, as they are covered by other health insurance schemes. This study was based on patients hospitalized for the first time for acute heart failure, but some of them probably already had a diagnosis of chronic heart failure: 42% had had at least one BNP assay during the previous year and 19% were already treated with an aldosterone antagonist. The possibility of first hospitalizations before 2006 (i.e. > 3 years before the inclusion period of this study) cannot be eliminated. One-year and 5-year mortality rates of 20—30% and 45—60%, respectively, have been reported [1]. The bias is therefore limited. The data used in this study were derived from medical and administrative databases that collect only limited clinical information, such as those necessary for the distinction between systolic and diastolic heart failure, which is one of the major limitations of this study. These databases also have the classical limitations concerning the validity of data collection and data coding in an ''administrative way'',

such as coding of diagnoses and chronic disease. Nevertheless, the exhaustiveness of this database can be considered to be good, as this information is required for reimbursement. Estimation of chronic disease status using ALD could be underestimated because the 100% reimbursement of healthcare expenditure is not useful for institutionalized people, those with mutual insurance or those with a pre-existing ALD. Some frequencies could be underestimated, especially for laboratory assays performed in public hospitals or reimbursement of certain medicinal products when they are dispensed during a stay in an institution.

Conclusions

Short-term and medium-term readmission and mortality rates after a first hospitalization for heart failure are extremely high. Despite the limitations of the databases used for this study, there still appears to be room for improvement in the drug treatment prescribed on discharge, in terms of frequency and combination therapies, in order to lower the readmission rate. Physicians managing these patients must prescribe recommended medicinal products at effective doses, while stressing the importance of adherence, and they must therefore provide attentive patient education concerning the presence of possible risk factors for decompensation. As mentioned in the introduction, disease management programmes have been demonstrated to be effective in many trials, in terms of readmission rates and quality of life, and are therefore now included in clinical practice guidelines. The French national health insurance fund (CNAMTS) is currently developing a return-home and follow-up management programme (PRADO) for patients hospitalized for heart failure, in partnership with general practitioners.

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